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[Title]

A PROCESS FOR PRODUCING BLOOD COAGULATION VII FACTOR  
AND/OR ACTIVATED BLOOD COAGULATION VII FACTOR

[Abstract]

[Object] There are provided a method of separating FVII and/or FVIIa from an FVIIa-ATIII complex and a process for producing FVII and/or FVIIa, based on said method.

[Constitution] A solution containing FVII and/or FVIIa is developed and adsorbed on anion-exchange resin and eluted with a  $\text{Ca}^{2+}$ -containing solution whereby FVII and/or FVIIa is separated from an FVIIa-ATIII complex.

[Claims]

[Claim 1] A method of separating blood coagulation VII factor (hereinafter, also called FVII) and/or activated blood coagulation VII factor (hereinafter, also called FVIIa) from an activated blood coagulation VII factor-antithrombin III complex (hereinafter, also called FVIIa-ATIII complex), which comprises developing a solution containing FVII and/or FVIIa on anion-exchange resin.

[Claim 2] A separation method according to claim 1 wherein after the solution containing FVII and/or FVIIa contaminated with the FVIIa-ATIII complex is developed on anion-exchange resin, the FVIIa-ATIII complex is adsorbed on the anion-exchange resin, and FVII and/or FVIIa is eluted from, or passed through, the resin whereby FVII and/or FVIIa is isolated and

purified.

[Claim 3] A separation method according to claim 2 wherein a  $\text{Ca}^{2+}$  source is contained in the buffer for permitting FVII and/or FVIIa to be eluted from or to pass through the resin, and its concentration is less than 40 mM.

[Claim 4] A separation method according to claim 2 or 3 wherein the pH value of the buffer for permitting FVII and/or FVIIa to be eluted from or to pass through the resin is 10.0 or less.

[Claim 5] A process for producing blood coagulation VII factor and/or activated blood coagulation VII factor, which comprises a step based on the separation method described in any of claims 1 to 4.

[Claim 6] A composition of blood coagulation VII factor and/or activated blood coagulation VII factor, which is substantially free of the FVIIa-ATIII complex.

[Claim 7] A composition of blood coagulation VII factor and/or activated blood coagulation VII factor according to claim 6, which is obtained in the process described in claim 5.

[Means to Solve the Problem] The present inventors extensively studied and examined to achieve removal of the FVIIa-ATIII complex from an FVII fraction, and as a result, they arrived at the present invention. The present invention provides a method of purifying FVII and/or FVIIa wherein a solution containing FVII and/or FVIIa suspected of being contaminated with the FVIIa-ATIII complex is prepared such that its  $\text{Ca}^{2+}$  concentration is 40 mM or less and its pH value is 10.0 or less,

and this solution is developed on anion-exchange resin and eluted with a buffer containing 40 mM or less  $\text{Ca}^{2+}$  with a pH value of 10.0 or less, whereby FVII and/or FVIIa is purified. Highly purified FVII and/or FVIIa can be prepared by use of the separation method provided by the present invention.